Period and Cohort Factors in the Incidence of Malignant Melanoma in the State of Connecticut

by James J. Collins* and Nancy Devine†

The reasons for the increase in both incidence and mortality from malignant melanoma are not clear at this time, although there is an indication of a "generation effect" in the increasing frequency of the disease. The application of an age-period-cohort model to incidence data on malignant melanoma for the State of Connecticut indicate that, unlike mortality, the increase is almost entirely related to period factors. Two explanations are provided to explain this pattern of period factor increase. First, the increase in incidence could be artifically produced by better and earlier diagnosis. Second, a decrease in ozone level in the atmosphere may be responsible for the increase.

The incidence of malignant melanoma has been increasing in Connecticut since at least 1935 (*1*) and has doubled in the U.S. in the last ten years (*2*), while mortality from this cancer has been increasing since at least 1950 (*3*). Figure 1 presents age standardized rates for malignant melanoma incidence and total skin cancer mortality for U.S. data arranged by calendar year. The reason for this increase in rates is not clear at this time. Cohort analyses of both incidence and mortality from malignant melanoma suggest the presence of a "generation effect" in the increasing frequency of the disease in western populations (*3–5*). More recently, two studies have considered both calendar year (period effect) and year of birth (cohort effect) simultaneously in the same model (*6,7*). These period-cohort analyses conclude, as did the cohort analyses, that the major factor behind the current increase in the mortality from malignant melanoma was the systematic increase in the rates for later birth cohorts. These studies, however, focused only on mortality. The purpose of this paper is to perform an age-period-cohort analysis on incidence data for the state of Connecticut to determine if the cohort hypothesis is also appropriate for incidence data.

Materials and Methods

Age-specific incidence rates in 5-year age groups for 5-year periods for malignant melanoma were provided by the Connecticut Tumor Registry. The years covered by the registry are 1935–1939 to 1970–1974. Only the age groups 20 to 24 to 80 to 84 are included in the analysis. Incidence for ages below age 20 are too low to produce stable rates and are therefore excluded from the analysis.

One approach for separating period and cohort effects from age patterns of incidence or mortality over time is presented by Sacher (*8,9*). He proposed both a biological-grounded model for the mortality process (*8*) and a method based upon this model for separating the
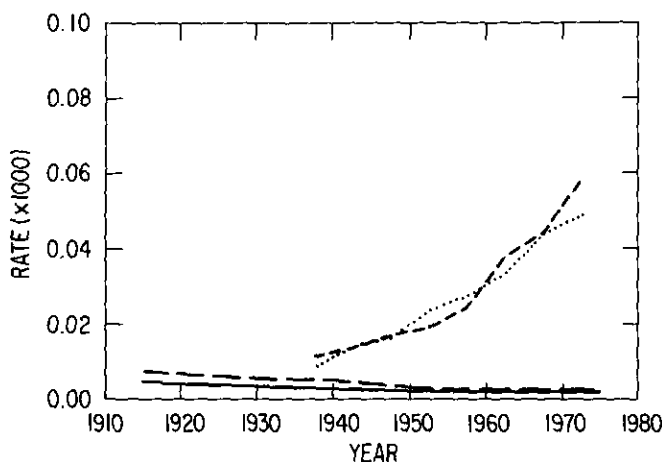

FIGURE 1. Age-standardized rates by sex for malignant melanoma incidence and total skin cancer mortality for the United States: (...) Connecticut male incidence; (- -) Connecticut female incidence; (—) U.S. white male mortality; (— —) U.S. White female mortality. Rates computed for total skin cancer mortality and prior to 1933 refers to the Death Registration States.

*American Cyanamid Company, Wayne, NJ 07470.
†Division of Biological and Medical Research, Argonne National Laboratory, Argonne, IL 60439.

three effects (9). Using this model as a basis for separation of age, period, and cohort effects, Sacher presented the expression:

$$M_{ij} = A_i + P_j + C_k + e_{ij} \qquad (1)$$

where M_{ij} is the logarithm of the age-specific mortality rate for age i and calendar year j, A_i is the age factor for the ith age level, P_j is the period factor for the jth calendar year, C_k is the cohort factor for the kth birth cohort, and e_{ij} is a random error term.

While the statement of an age-period-cohort model is straightforward, the operationalization of the function leads to at least three major problems. These problems are (1) what is a realistic form of the function, (2) what method will be used to overcome the identification problem and, (3) to what extent does multicollinearity affect the solution. These problems are dealt with in detail in other sources (10), and a full exposition is beyond the scope of this presentation. Results of age-period-cohort analyses must be interpreted cautiously because of inherent instability in the solution. We proceed with this caveat in mind.

A solution for the values of the factors can be obtained from a long-running series of age-specific incidence rates by periods of measurement where the interval of the ages and the periods are equal. Three separate solutions for the age, period and cohort model were used. The first is essentially Sacher's solution, where the cohort effect prior to 1860 is constrained to zero. There is some historical evidence that this constraint is reasonable (10). The second solution uses the age pattern of melenoma mortality corrected for cohort effects for Australian males and females as presented by Holman et al. (7). This method makes the incidence matrix of full rank and thus allows a unique solution. This set of constraints assumes that Australian and Connecticut populations have the same age pattern of melenoma and that there is no age difference in survival patterns of the disease. This second assumption may be problematic since these is evidence that relative survival rates for melanoma decrease with age (11). The final solution employed a maximum eigenvalue least-squares approach (10).

In this approach, a series of principal components is estimated from the correlation matrix of the original incidence matrix and the components with small eigenvalues are eliminated. The criterion for elimination of principal components was based upon the condition index (12). The principal components were then translated into the original variables to provide the necessary parameter estimates.

The first solution based on historical evidence, the second based upon a previous study and the third based upon a mathematical decision, yield very similar results, thus providing some support for each set of constraints. Each of these models fit the data equally well, explaining 95% of the variance. For the sake of brevity, only the results of third solution will be discussed.

Results

Figure 2 presents the age pattern for the age-period-cohort model. The pattern for both males and females is very similar: that is, low at age 20, increasing to a peak at age 50, and then becoming stable. This age pattern for melanoma has been previously documented (13). It should be noted that the age pattern for incidence is less steep at the older ages than the age pattern for mortality. One possible explanation may be the increase in case-fatality with age (6).

The pattern for the period effect is shown in Figure 3. The steady increase in the period factor over time indicates that a large part of the increase in incidence of melanoma may be related to period factors. The cohort factor is presented in Figure 4. Compared to the period factor, there is little change over time in the cohort factor. The cohort factor peaks around 1850 and then drops to a low around 1900 after which there is a slight increase to the present. This increase from 1900 to the present corresponds with the conclusions of Houghton (1) for the same data. In general, however, the cohort factor displays less influence on melanoma incidence than does the period factor.

To provide an estimation of the relative contribution of period and cohort effects, we can estimate age standardized incidence rates from the original model formulation in the absence of period effects. This is done by using the original model formulation presented in Eq. (1) ignoring the error terms to construct the estimated age-specific incidence rates (M_{ij}) for age, period and cohort factors considered simultaneously, or

$$M_{ij} = A_i + P_j + C_k \qquad (2)$$

and also that for age and cohort effects, or,
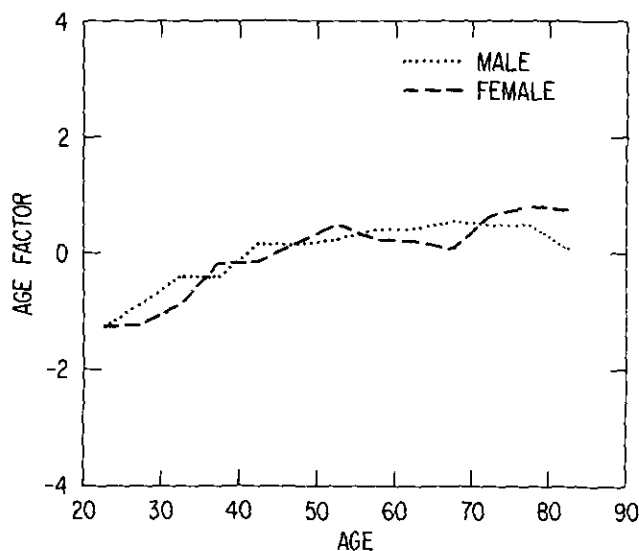
$$M_{ij} = A_i + C_k \qquad (3)$$

FIGURE 2. Age factor by sex of the age-period-cohort model for incidence of malignant melanoma for Connecticut.
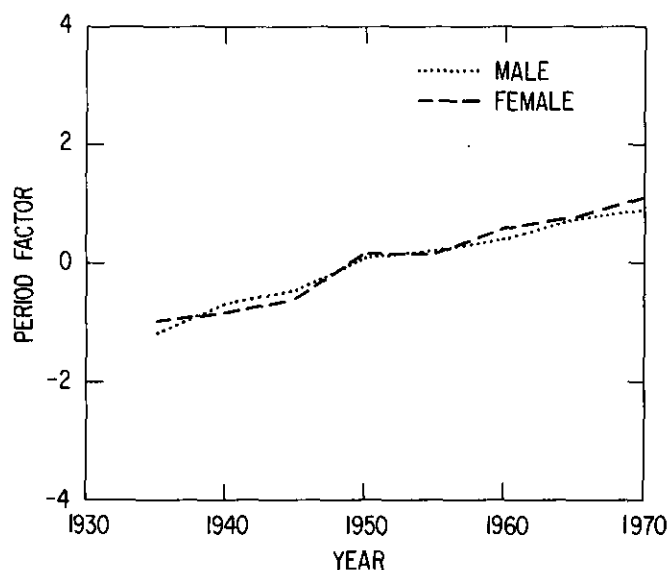
FIGURE 3. Period factor by sex of the age-period-cohort model for incidence of malignant melanoma for Connecticut.
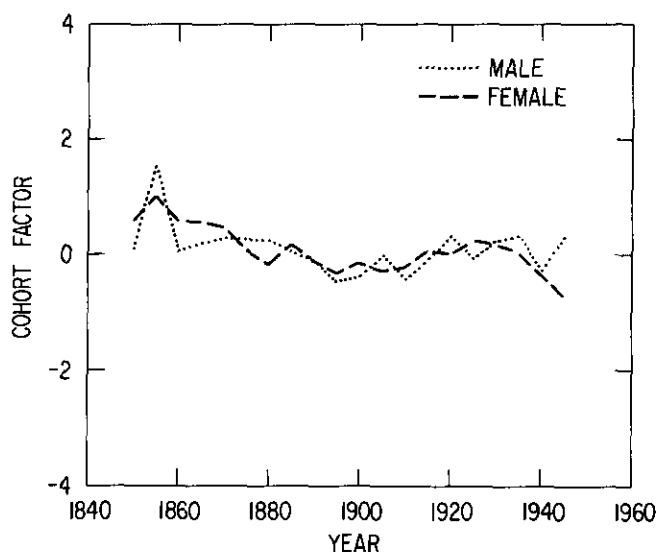

FIGURE 4. Cohort factor by sex of the age-period-cohort model for incidence of malignant melanoma for Connecticut.

This latter equation, when compared to Eq. (2) will provide a rough estimate of the contribution of period factors to the increasing incidence of melanoma over time.

Age standardized incidence rates (ASIR) are computed from the age-specific incidence rates estimated from Eqs. (2) and (3). The actual data is also presented. In Table 1, the actual ASIR is 0.008286 in 1935 to 1939 and rises to 0.048759 in 1970 to 1974 or an increase of 488%. The estimated ASIR computed from the age, period, cohort model is presented in the second equation in Table 1. The ASIRs are slightly higher than the actual data but the increase is very similar. Equation (3), or the estimated ASIR in the absence of period effects, shows virtually no increase in the ASIR when period effects are ignored. Indeed, there appears to be a slight decrease in incidence from 1935 to 1970 if only age and cohort factors are considered. It seems reasonable, therefore, that explanations for the rise in incidence of melanoma in the state of Connecticut should focus on period factors.

Discussion

There are two sets of arguments that may be used to explain the rather large period components in the incidence data. First, it could be argued that the period effect represents a real increase in the incidence of the disease. An argument that has been made, for instance, is that a decrease in the ozone level in the atmosphere may be responsible for the increase (14). For this to be true, however, at least for the state of Connecticut, the latency between exposure and appearance of the disease would have to be very short, that is 5 years or less to produce the period effect. A longer latency in the presence of increasing exposure would be reflected in the age-period-cohort model as both period and cohort effects. This results because each new birth cohort would be exposed to higher levels of the environmental carcinogen and would thus have higher probabilities of developing malignant melanoma than would older birth cohorts.

A second possible explanation for the increase is that it is an artifact of how the data were collected and how the disease was diagnosed. Incomplete registration of

Table 1. Actual and estimated age-standardized incidence rates ($\times$ 1000) for females in Connecticut for 1935 to 1939 and 1970 to 1974.

Equation	Incidence		Absolute change	% change
	1935–39	1970–74		
(1) Actual data $M_{ij} = A_i + P_j + C_k + e_{ij}$	0.008286	0.048759	+ 0.040473	+ 488
(2) Estimated full model $M_{ij} = A_i + P_j + C_k$	0.008537[a]	0.05385	+ 0.045313	+ 531
(3) In the absence of period effects $M_{ij} = A_i + C_k$	0.008537[a]	0.007275	−0.001262	−14

[a] The reason for the exact agreement between (2) and (3) for the time period 1935–39 is that the period effect is contained to zero for that year in Eq. (2). This constraint does not affect the form of the function obtained.

Table 2. Stage distribution for patients diagnoses 1950 to 1969 from the program for cancer surveillance, epidemiology and end results reporting (SEER).

	1950–54	1955–59	1960–64	1965–69
Number classified				
Localized	372	588	937	1141
Regional	120	132	163	188
Distant	120	105	177	156
Unknown	53	53	81	78
Total	665	878	1358	1563
Percentage				
Increase of all classifications	—	32	204	235
Portion of total increase attributed to increase in localized	—	101	73	100

melanoma is probably responsible for some of period effect even though most researchers would argue that this effect is probably very small (*3–5*). There is also the possibility that improving diagnosis over time has artificially increased the incidence. Melanoma of the skin is a rare tumor. More accurate diagnosis may increase the number of tumors classified as melanoma. Early diagnosis may also increase incidence (*15*). Table 2 presents the stage distribution by year for patients diagnosed from the SEER Program (*11*). The Connecticut registry represents 40% of the SEER population. The total diagnoses for melanoma increased from 665 in 1950 to 1954 to 1563 in 1960 to 1969 representing a 235% increase in the diagnosis of the disease. This corresponds to the increase in incidence in Figure 1. Virtually all of this increase appears to be related to the increase in diagnosis of localized melanoma. These data indicate that incidence increase in melanoma is related to an increase in the localized stage of the disease. Earlier diagnoses may, therefore, account for the current increase in the disease. It does appear that at least part if not all of the period effect associated with the increase in melanoma may be attributed to an artifact of how the data were collected over time.

Age-period-cohort analyses, when applied to both incidence and mortality data, can provide important indications of the etiology of disease under study. The commonly cited explanation for increases in melanoma is the change in clothing and recreation trends since World War II. In the present analysis, the dominance of a period effect indicates a causative factor operating on all age groups equally rather than one operating at an early age, as with cohort effects.

Though sunlight is known to be an important cause of melanoma, research findings indicate that it is not the only causative mechanism. Clinically, melanomas are less concentrated in sun-exposed body sites than are nonmelanomas. (*16*). Furthermore, studies in Australia show a higher incidence for members of professional and managerial classes living in urban areas than those involved in outdoor work (*17*). The commonly proposed

hypothesis is that of the importance of acute, intermittent exposure to ultraviolet light rather than chronic exposure in melanoma incidence. (*13*). This is particularly relevant for those sex-specific sites displaying the greatest increases in rates, that is the lower limb in females and trunk in males, which show lack of a strong age dependence (*1*). However, it is also possible that secular increases in an environmental pollutant, such as atmospheric pollution, which would accompany the trend toward urbanization and affluence of lifestyle and act on all age groups, are an important contributor to the observed increased melanoma incidence. This would also be plausible in light of the similarities of these increases through time in both sites (*18*).

The cohort effect, though small, is still of importance. As stated earlier, increased incidence and mortality from melanoma have most commonly been regarded as largely birth cohort phenomena. In the present study the period effect dominated but the presence of cohort effect in the incidence of malignant melanoma for the state of Connecticut is unmistakable. However, the effects are both fluctuating and of small magnitude.

Conclusion

Mortality and incidence for malignant melanoma have most often been considered largely a cohort phenomena. In the present study, however, incidence of melanoma for the state of Connecticut appears to have a large period component accounting for virtually all of the increase in this disease over the past 35 years. While there is a cohort component, the period component does dominate. However, these results are based on limited data and the etiologic implications of a period factor in the rise in melanoma incidence, should be examined in other data bases.

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